

Mastoiditis, Lymphoma, and AIDS

THOMAS LOWRY
LAIQ RAJA, MD
ABRAHAM VERGHESE, MD
El Paso, Texas

THE INCIDENCE OF mastoiditis has decreased in recent decades because of the availability of oral antibiotics and better treatment of acute otitis media.^{1,2} In the era of the acquired immunodeficiency syndrome (AIDS), however, there has been a resurgence of conditions that before this were fairly uncommon. One group of authors has noted that the frequency of head and neck manifestations in patients with AIDS is nearly 100% during the course of their disease.³ In addition, many authors have observed an increase in the incidence and prevalence of serous otitis media, acute otitis media, and external otitis,¹⁻⁶ but reports of mastoiditis in patients with AIDS appear less frequently.

In addition to traditional T-cell pathogens, it is now well recognized that persons infected with the human immunodeficiency virus (HIV) also have B-cell defects and problems with pathogens such as *Streptococcus pneumoniae*. Sinusitis, bacterial pneumonia, and even bronchiectasis have been described in these patients.⁷

We describe the cases of two patients with AIDS and B-cell lymphoma who presented with mastoiditis.

Report of Cases

Patient 1

The patient, a 35-year-old HIV-positive man, presented to the emergency department at Thomason Hospital, El Paso, Texas, with severe right-sided ear pain for two weeks. The patient described the pain as throbbing, with radiation to his face and jaw. He did not have blurred vision, vertigo, or drainage of fluid from his ear but did have a global headache. Two weeks before this, the patient was diagnosed with acute otitis media and was treated with a course of amoxicillin and clavulanate potassium, 500 mg three times a day, but his symptoms have only worsened since then. He had been diagnosed with HIV ten years previously, and his most recent CD4⁺ cell count was 152×10^6 per liter (152 cells per μ l). His medical history was notable for non-Hodgkin's B-cell lymphoma, *Mycobacterium avium-intracellulare*, genital herpes, anal condylomata, and a persistent perirectal fistula. Medications at admission included zidovudine, acyclovir, and the combination of trimethoprim and sulfamethoxazole.

On physical examination, the patient's temperature was 36.9°C (98.4°F), his blood pressure was 132/96 mm of mercury, his pulse rate was 94 beats per minute, and respirations were 20 per minute. An injected tympanic membrane was noted with no discernible air-fluid level

or perforation. Tenderness was elicited on palpation of the right mastoid and preauricular areas, and a mild cervical lymphadenopathy was present. The findings of the physical examination were otherwise unremarkable. The leukocyte count was 4.18×10^9 per liter (4,180 per μ l) (0.29 [29%] segmented neutrophils, 0.01 [1%] band forms, 0.55 [55%] lymphocytes, 0.09 [9%] monocytes, and 0.01 [1%] eosinophils). The results of serum chemistry studies were remarkable only for an elevated alkaline phosphatase level of 115 U per liter and a lactate dehydrogenase level of 241 U per liter. No specimens were taken for culture, and tympanocentesis was not performed, but computed tomography of the head showed asymmetry and increased bony densities of the right mastoid, consistent with chronic mastoiditis.

The patient was placed on a two-week course of amoxicillin-clavulanate, 500 mg every eight hours, and ciprofloxacin, 500 mg twice a day. He showed clinical improvement in his signs and symptoms in the ensuing weeks. Three weeks later, the patient presented with facial pain and right seventh nerve paralysis; magnetic resonance imaging showed a nasopharyngeal mass that on biopsy was a B-cell lymphoma. The patient declined radiation therapy and died two months later.

Patient 2

The patient, a 36-year-old HIV-positive woman, was admitted to Thomason Hospital for gradually worsening right ear pain beginning one day before admission. The patient described the pain as a stabbing pressurelike sensation in her ear and mastoid region, but did not have any discharge, tinnitus, or hearing loss. She also had a generalized headache with intermittent sensations of disequilibrium, nausea, and fever with chills. The patient was diagnosed with HIV infection 14 months before this admission, and her most recent CD4⁺ count was 84×10^6 per liter (84 cells per μ l). Since being diagnosed with HIV, she has had several episodes of acute sinusitis and right otitis media. Her medications at the time of admission included didanosine, trimethoprim-sulfamethoxazole, and acyclovir.

On physical examination, the patient's temperature was 41.1°C (106.0°F), her blood pressure was 115/65 mm per mercury, her pulse rate was 125 beats per minute, and respirations were 18 per minute. She had a bulging and injected right tympanic membrane with obliteration of the bony structures. An air-fluid level behind the tympanic membrane was not discernible, and no perforation was present. The external auditory meatus and mastoid region were tender to palpation, but no gross anatomic deviations or swelling was evident. The leukocyte count was 4.27×10^9 per liter (4,270 per μ l) (0.68 neutrophils, 0.09 band forms, 0.21 lymphocytes, and 0.02 monocytes) and the cerebrospinal fluid showed a leukocyte count of 8×10^6 per liter (8 per μ l) with no organisms present. Cultures done of tympanocentesis, cerebrospinal fluid, and blood specimens were all sterile, and the results of the rest of the laboratory workup were unremarkable.

The patient was diagnosed with recurrent otitis media and mastoiditis and treated with ticarcillin and clavulanate, 3.1 grams intravenously every six hours. A marked improvement was noted by the ninth hospital day, and she was discharged home with a two-week course of ceftazidime, 2 grams given intravenously every twelve hours. Following discharge, the patient's condition remained stable for two months when she had the abrupt onset of right ear pain, fever, and signs of sepsis. A computed tomographic scan of the head revealed clouding of the right mastoid air cells, and culture of the middle ear fluid grew *S pneumoniae*. A right mastoidectomy was performed without complications. The patient received intravenous ceftriaxone sodium, 1 gram intravenously every 24 hours for the following 10 days, and her condition gradually improved. Two months later, she presented with anemia and neutropenia and was ultimately diagnosed with B-cell non-Hodgkin's lymphoma, presenting as an abdominal mass. Studies were not performed to look specifically for a nasopharyngeal mass. She died two months after the diagnosis of lymphoma.

Discussion

Acute mastoiditis usually follows an episode of acute suppurative otitis media, with the pathologic events being, first, obstruction and sequestration of infection at the additus ad antrum and the smaller air cell tracts and, then, temporal or mastoid bone remodeling followed by bone resorption and decalcification.¹

The pathogenesis of chronic mastoiditis is similar to that of acute disease, with obstruction of the eustachian tube being a more prominent feature.^{1,3,5,6,8} The causal agents are usually bacterial with *S pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis*, and occasionally anaerobes being isolated most frequently.^{1,4,3,9}

In patients with AIDS, however, alterations in normal immune function and middle ear anatomy may play a role in the development of middle ear infections, including mastoiditis. The most consistent finding is poor eustachian tube function due to such factors as HIV-related adenoidal hyperplasia and hypertrophy, recurrent respiratory tract viral infection, viral-induced allergy, and nasopharyngeal masses.^{3,5,6,8} Patients with HIV infection also have measurable B-cell dysfunction, neutrophil dysfunction, spontaneous B-cell proliferation with a nonspecific polyclonal increase in immunoglobulin G secretion, and a failure to respond to a variety of de novo antigenic stimuli.⁷

Several studies have described the histopathologic findings in the temporal bones of patients infected with HIV and who have AIDS.^{2,10,11} Michaels and co-workers noted histologic evidence of severe otitis media in 20% of patients studied and low-grade otitis media in 60% of their patients.² Although they noted no clinical cases consistent with mastoiditis, radiographs of microslides indicated markedly increased density of mastoid bone and a diminished number of air cells.²

Haversian systems were found to be highly irregular in pattern in a number of specimens.² Davis and associates studied the temporal bones of 13 patients with AIDS and found histologic evidence of acute otitis media in 4 patients (31%), chronic otitis media in 2 patients (15%), and serous otitis media in 3 patients (23%).¹⁰ No descriptions of disease in mastoid bones were noted. In contrast to these studies, the histopathologic changes described by Chandrasekhar and colleagues were significant in that 7 of the 8 bone specimens analyzed demonstrated some form of petromastoiditis.¹¹ Two of the studies were of the temporal bones of patients with documented AIDS,^{2,10} and the third was of HIV-positive patients not described as having AIDS.¹¹ In our review of the literature, we found accounts of 12 patients with HIV infection or AIDS and mastoiditis.^{3,5,12-16} Although the incidence of mastoiditis has decreased over the past several decades,^{1,17} no objective data exist on the incidence or prevalence of the disease in patients with AIDS. Information regarding the frequency rate of complications, responses to therapeutic intervention, and prognostic implications of mastoiditis in AIDS patients is also lacking. Of note, the two patients presented here followed different courses, with one responding well to standard antibiotic therapy and long-term sequelae developing in the other that ultimately required surgical therapy.

That both patients had B-cell non-Hodgkin's lymphoma is also important because a nasopharyngeal mass may have contributed to the pathogenesis of their disease. Carbone and co-workers retrospectively studied 82 patients with HIV-related non-Hodgkin's lymphoma.¹⁸ Of the 82 patients, 15 (21%) had primary head and neck and 13 (18%) had systemic head and neck non-Hodgkin's lymphoma. Of 15 patients with primary head and neck disease, 7 (47%) presented with extranodal disease in the absence of any demonstrable disease in the lymph nodes; 11 patients (73%) had involvement of the Waldeyer's ring; 5 patients (33%) had involvement of the head and neck soft tissue; 3 patients (20%) each had involvement of the maxillary region (gum of the maxillary sinus and bones) and palate; 2 patients (13%) each had involvement of the hypopharynx, gum, and skin; and 1 patient (7%) had involvement of the epiglottis, uvula, floor of the mouth, parotid, orbit, hyoid bone, and retromolar trigone. From the clinical point of view, the stage distribution was the only statistically significant difference in the two groups (primary head and neck versus systemic head and neck non-Hodgkin's lymphoma) of the head and neck lymphoma ($P < .001$). Of 15 patients with primary head and neck non-Hodgkin's lymphoma, 10 (67%) had stages I and II, whereas all the patients with systemic head and neck non-Hodgkin's lymphoma had stages III and IV.

Shapiro and colleagues described 20 patients with AIDS in whom non-Hodgkin's lymphomas developed in the head and neck region.¹⁹ The tumor was observed in a variety of sites, including the nasopharynx, orbit, parotid, maxillary sinus, submandibular triangle, arteri-

or and posterior cervical triangles, supraclavicular fossa, and the hypopharynx. Nine cases of oral non-Hodgkin's lymphoma occurring in homosexual male HIV-infected patients were evaluated by Green and Evasole.²⁰ The lymphomas were located in the maxillary or mandibular gingiva (3 patients), palate (2 patients), mandible, lateral tongue, tonsillar pillar, and retromolar pad. Carbone and associates concluded in their study that head and neck non-Hodgkin's lymphoma in HIV-infected patients represents a significant proportion (39%) of the HIV-related lymphomas.²¹ Most patients with head and neck non-Hodgkin's lymphoma had severe immunodeficiency, extranodal disease, aggressive histologic findings, and a poor treatment response.²¹⁻²³

The two cases reported here underscore the importance of being aware of mastoiditis in a patient with AIDS. That both patients also had lymphoma suggests that this association may not be casual; clinicians should keep lymphoma and an occult nasopharyngeal mass in mind when seeing HIV-infected patients who present with mastoiditis.

REFERENCES

- Nadol JB Jr, Eavey RD. Acute and chronic mastoiditis: clinical presentation, diagnosis, and management. *Curr Clin Top Infect Dis* 1995; 15:204-229
- Michaels L, Soucek S, Liang J. The ear in the acquired immunodeficiency syndrome: I. temporal bone histopathologic study. *Am J Otol* 1994; 15:515-522
- Lalwani A, Sooy CD. Otologic and neurotologic manifestations of acquired immunodeficiency syndrome. *Otolaryngol Clin North Am* 1992; 25:1183-1195
- Madriz J, Herrera G. Human immunodeficiency virus and acquired immune deficiency syndrome AIDS-related hearing disorders. *J Am Acad Audiol* 1995; 6:358-364
- Kohan D, Rothstein SG, Cohen NL. Otologic disease in patients with acquired immunodeficiency syndrome. *Ann Otol Rhinol Laryngol* 1988; 97(6 pt 1):636-639
- Sooy CD. The impact of AIDS on otolaryngology-head and neck surgery. *Adv Otolaryngol Head Neck Surg* 1987; 1:1-28
- Verghese A, al-Samman M, Nabhan D, Naylor AD, Rivera M. Bacterial bronchitis and bronchiectasis in human immunodeficiency virus infection. *Arch Intern Med* 1994; 154:2086-2091
- Hadderingh R, Tange R, Danner S, Schattenkerk J. Otorhinolaryngological findings in AIDS patients: a study of 63 cases. *Arch Otorhinolaryngol* 1987; 244:11-14
- Rodriguez Barradas MC, Musher DM, Hamill RJ, Dowell M, Bagwell JT, Sanders CV. Unusual manifestations of pneumococcal infection in human immunodeficiency virus-infected individuals: the past revisited. *Clin Infect Dis* 1992; 14:192-199
- Davis LE, Rarey KE, McLaren LC. Clinical viral infections and temporal bone histologic studies of patients with AIDS. *Otolaryngol Head Neck Surg* 1995; 113:695-701
- Chandrasekhar SS, Siveris V, Sekhar HK. Histopathologic and ultrastructural changes in the temporal bones of HIV-infected human adults. *Am J Otol* 1992; 13:207-214
- Gherman CR, Ward RR, Bassis ML. *Pneumocystis carinii* otitis media and mastoiditis as the initial manifestation of the acquired immunodeficiency syndrome. *Am J Med* 1988; 85:250-252
- Strauss M, Fine E. Aspergillus otomastoiditis in acquired immunodeficiency syndrome. *Am J Otol* 1991; 12:49-53
- Shepp DH, Tang IT, Ramundo MB, Kaplan MK. Serious *Pseudomonas aeruginosa* infection in AIDS. *J Acquir Immune Defic Syndr* 1994; 7:823-831
- Linstrom CJ, Pincus RL, Leavitt EB, Urbina MC. Otologic neurotologic manifestations of HIV-related disease. *Otolaryngol Head Neck Surg* 1993; 108:680-687
- Kohan D, Hammerschlag PE, Holliday RA. Otologic disease in AIDS patients: CT correlation. *Laryngoscope/Otologic Disease and AIDS* 1990; 100:1326-1330
- Chui R. Otitis media. *Common Problems of the Head and Neck Region* 1982; 9:211-225
- Carbone A, Vaccher E, Barzan L, Gloghini A, Volpe R, De Re V, et al. Head and neck lymphomas associated with human immunodeficiency virus infection. *Arch Otolaryngol Head Neck Surg* 1995; 121:210-218
- Shapiro AL, Shechtman FG, Guida RA, Kimmelman CP. Head and neck lymphoma in patients with the acquired immune deficiency syndrome. *Otolaryngol Head Neck Surg* 1992; 106:258-260
- Green TL, Eversole LR. Oral lymphomas in HIV infected patients: association with Epstein-Barr virus DNA. *Oral Surg Oral Med Oral Pathol* 1989; 67:437-442
- Carbone A, Tirelli U, Vaccher E, Volpe R, Gloghini A, Bertola G, et al. A clinicopathologic study of lymphoid neoplasias associated with human immunodeficiency virus infection in Italy. *Cancer* 1991; 68:842-852
- Knowles DM, Chamulak GA, Subar M, Burke JS, Dugan M, Wernz J, et al. Lymphoid neoplasia associated with the acquired immunodeficiency syndrome (AIDS): the New York University Medical Center experience with 105 patients (1981-1986). *Ann Intern Med* 1988; 108:744-753
- Lowenthal DA, Straus DJ, Campbell SW, Gold JW, Clarkson BD, Koziner B. AIDS-related lymphoid neoplasia: the Memorial Hospital experience. *Cancer* 1988; 61:2325-2337